UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,538	09/19/2006	Ippei Sakimoto	06659/LH	9964

1933 7590 04/22/2008

FRISHAUF, HOLTZ, GOODMAN & CHICK, PC
220 Fifth Avenue
16TH Floor
NEW YORK, NY 10001-7708

EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
4131	

MAIL DATE	DELIVERY MODE
04/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,538	SAKIMOTO ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *19 September 2006, 31 January 2007, 23 February 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a National Stage entry of PCT/JP05/11630 filed on 24 June 2005 and claims priority to Japan foreign application no. 2004-374445 filed on 24 December 2004 and Japan foreign application no. 2004-186480 filed on 24 June 2004. Certified copies of the foreign priority documents in Japanese have been received.

The preliminary amendment filed on 5 October 2006 in which claims 1-8 were cancelled, and claims 9-16 were newly added, is acknowledged.

Information Disclosure Statement

The information disclosure statements (IDS) dated 19 September 2006, 31 January 2007 and 23 February 2007 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, they have been placed in the application file and the information therein has been considered as to the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of squamous carcinoma, does not reasonably provide enablement for the treatment of other types of cancers. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn towards the method for treating cancers by administering to a subject in need thereof an effect amount of a radiosensitizer in combination with radiation.

Breadth of claims: The claims are extremely broad in that they encompass literally the treatment of all types of cancers.

Amount of guidance/Existence of working examples: Working examples are present which show that the compounds claimed are effective against squamous carcinoma cells. However, there is no guidance in the specification, nor are there any working examples, to show that the claimed compounds are effective against other types of cancers, such as adenocarcinoma cancer.

State of the prior art/Predictability or unpredictability of the art: The prior art teaches that the claimed compounds are useful as an anticancer agent (US Patent No. 6,518,410 B2). These compounds are effective in the treatment of colon cancer, lung cancer and gastric cancer (US Patent No. 6,518,410 B2). However, there is no prior art which teaches that the claimed compounds can treat other classes of cancer. Moreover, Park *et al.* teaches that radiotherapy is only effective in treating only specific kinds of cancers such as lung cancer, mammary cancer, and uterine cancer, while some other kinds of cancers show only partial effects or develop resistance to radiotherapy (PTO-892, ref. C, paragraph 0004)

Therefore, in view of the *Wands* factors as discussed above, there is no clear and convincing evidence in sufficient support of the use of the claimed compounds for the treatment of all types of cancers.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,518,410 B2 to Yamazaki *et al.* (herein referred to as the '410 patent), published US patent application no. 2004/0181114 A1 by Hainfeld *et al.*, and published US patent application no. 2003/0166692 A1 by Park *et al.*

The '410 patent discloses sulfoquinovosylacylglycerol derivatives that may be used as an immunosuppressive agent, anticancer agent, and DNA polymerase α inhibitor (abstract; column 2, lines 35-42). These compounds exhibit low toxicity and usability of long-term administration (column 2, lines 38-39). The sulfoquinovosylacylglycerol derivatives disclosed in the '410 patent have the structure as shown in formula (1-1). In formula (1-1), R_{101} represents an acyl residue of a higher fatty acid, wherein the acyl residues include groups represented by R-C(=O), where R

represents an alkyl or alkenyl group having 13 or more carbon atoms, preferably in the range of 13 or more and 25 or less (column 4, lines 21-34; claim 1). Additionally, the acyl group of R_{101} can be represented by the formula $CH_3(CH_2)_nCO$-, wherein n is an integer from 12-24, or having only an even number between 12-24 (claims 4, 21-22 and 24). This results in R_{101} having an acyl chain which contains an odd number of carbons, from 13-25. In formula (1-1), R_{102} represents a hydrogen atom or an acyl residue with the same independent meaning as those of the R_{101} group (column 4, lines 44-47; claim 1). The inhibitory activity of the various sulfoquinovosylacylglycerol derivatives are shown in table 7 (columns 37-38). The anti-cancer activity of various sulfoquinovosylacylglycerol derivatives against colon cancer cells and gastric cancer cells is shown in tables 8 and 9, respectively (columns 39-40). The '410 patent does not teach the method wherein the compounds are used in combination with irradiation to treat cancers.

Hainfeld *et al.* teaches methods for enhancing radiation effects with metal nanoparticles. Radiation has commonly been used as a method of treating cancers. However, a drawback to the treatment of cancers by radiation alone is that radiations are not generally very specific for the tumor (paragraph 0002). An alternative is the use of compounds that act in combination with radiation to produce an improved response, usually by making DNA more susceptible to radiation (paragraph 0003). These compounds are generally known as radiosensitizers. Some radiosensitizers are themselves anti-cancer chemotherapeutic drugs that appear to work synergistically with x-irradiation (paragraph 0004). Instead of compounds as radiosensitizers to enhance

radiation, another type of radiation enchancement method uses a metal surface, known as photoactivation. Hainfeld *et al.* provides methods of using metal nanoparticles to enhance the dose and effectiveness of x-rays or other kinds of radiation in therapeutic regimes of ablating a target tissue such as tumor (abstract; paragraph 0001).

Park *et al.* teaches a method of administering a composition comprising [N'-(phenyl-pyridin-2-yl-methylene)-hydrazine carbodithioic acid methyl ester] in combination with radiation for enhancing radiotherapy on cancerous cells or tumors (abstract; paragraph 0001; claims 10-11 and 13). Chemotherapy-radiotherapy combinations are administered to treat a variety of cancers, based on the theory that the mechanisms for each method, and their toxicities, do not overlap. The necessary conditions of candidate anticancer drugs that can also be used as radiotherapy-enhancing agents are 1) they enhance the anticancer effect of radiation therapy, 2) they cause no damage to normal cells, and 3) they have minimal toxicity (paragraph 0009). Park *et al.* indicates that [N'-(phenyl-pyridin-2-yl-methylene)-hydrazine carbodithioic acid methyl ester] is synergistically effective in treating cancerous cells or tumors when used in combination with radiotherapy, compared to irradiation only. Thus, a method for enhancing radiotherapy on cancers in mammals is provided, which comprise administering the effective amount of [N'-(phenyl-pyridin-2-yl-methylene)-hydrazine carbodithioic acid methyl ester] in combination with radiation (paragraph 0023). Preferably, [N'-(phenyl-pyridin-2-yl-methylene)-hydrazine carbodithioic acid methyl ester] is first administered, followed by irradiation.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the '410 patent, concerning sulfoquinovosylacylglycerol derivatives that may be used as immunosuppressive agents, anticancer agents, and DNA polymerase α inhibitors, with the teachings of Hainfeld *et al.*, regarding methods for enhancing radiation effects with compounds or metal nanoparticles, with the teachings of Park *et al.*, regarding a method for administering a composition comprising [N'-(phenyl-pyridin-2-yl-methylene)-hydrazine carbodithioic acid methyl ester] in combination with radiation for enhancing radiotherapy on cancerous cells or tumors. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Park *et al.*, and exemplified by Hainfeld *et al.*, that a combination treatment of chemotherapy-radiotherapy can mediate anti-cancer effects via different mechanisms. Thus, the said combination of cancer treatments, e.g. administering a sulfoquinovosylacylglycerol derivative in combination with irradiation, is expected to have synergistic effects on treating cancers since sulfoquinovosylacylglycerol derivatives are known to inhibit DNA polymerase α which controls DNA synthesis, thereby making it more susceptible to radiation. As Hainfeld *et al.* indicated, compounds that make DNA more susceptible to radiation can be used in combination with radiotherapy to enhance the radiation effects.

Absent of any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in treating cancers by combining the use of the anticancer sulfoquinovosylacylglycerol derivatives,

as disclosed in the '410, with the radiation therapy methods discussed by Hainfeld *et al.* and Park *et al.*

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang can be reached on 571-272-0562 and Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SCARLETT GOON/
Examiner
Art Unit 4131

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 4131